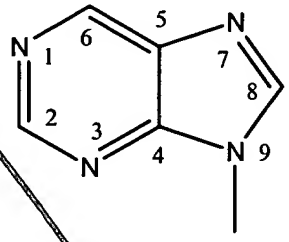
V and W together are a covalent bond; and

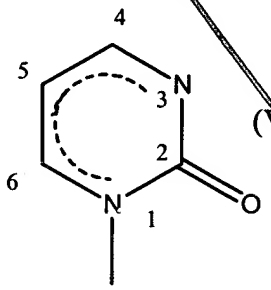
B is a purinyl moiety of Formula VI



(VI)

optionally substituted at position 2 with -OH, -SH, $-NH_2$ or halogen, at position 6 with Cl, $-NH_2$, -OH, or C_1-C_3 alkyl, and at position 8 with Br or I; or

B is a pyrimidinyl moiety of Formula VII



(VII)

substituted at position 4 with =O or NH_2 and optionally substituted at position 5 with halogen or C_1-C_3 saturated or unsaturated alkyl optionally substituted 1 to 3 times with halogen.

REMARKS

I. Status of the Claims

Claims 56-71, 95, 96 and 103-109 are pending. Claims 56-71, 95, 96, and 103-109 have been rejected.

Formula III of Claims 56 and 95 has been amended in an effort to better illustrate Applicants' claimed invention. Specifically, Formula III has been amended to delete the negative charge on the oxygen atom by adding a H atom and another oxygen atom has been added between the phosphorous and the Z moiety. Support for the latter amendment can be

found in the Specification on page 11, lines 1-7. The oxygen between the phosphorous and Z moiety was inadvertently omitted from the structure of Formula III. The Specification describes that the compound of Formula III substitutes a moiety Z for the alkyl-quarternary amine of the compounds of Formula I. No new matter has been added by the present amendments.

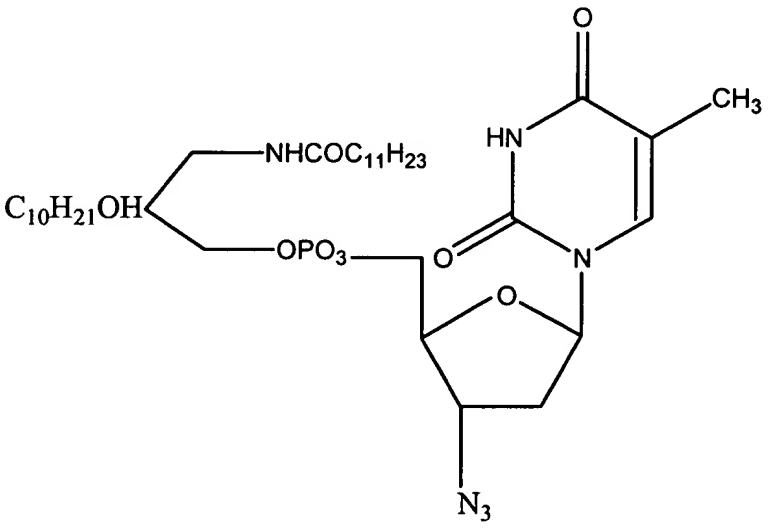
II. Rejection under 35 U.S.C. § 112, first paragraph

Claims 56-71, 95, 96, and 103-109 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

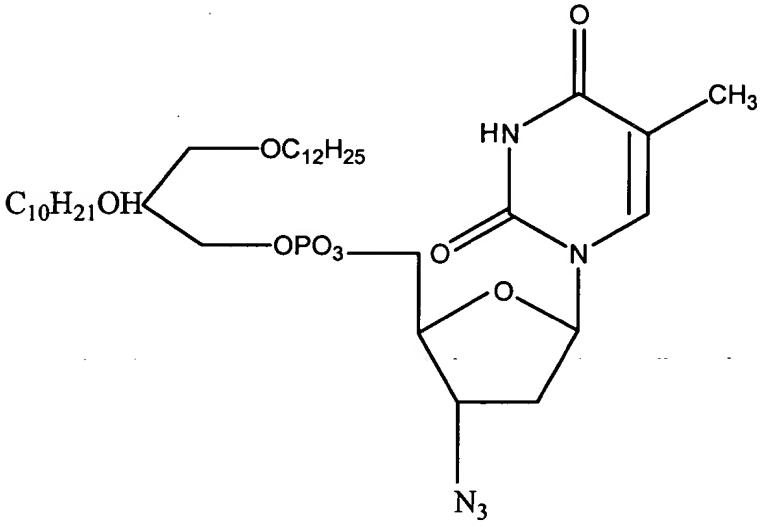
The standard for determining whether the specification meets the enablement requirement is that the claimed invention must be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands,* 858 F.2d 731, 737 (Fed. Cir. 1988). As described below, undue experimentation is not necessary for one skilled in the art to make and/or use Applicants invention.

The specification recites as an exemplary preferred compound of Formula III, as now amended in claims 56 and 95, 3'-azido-3'-deoxy-5'-(3-dodecanamido-2-decyloxypropyl)-phosphothymidine. Specification, page 13, lines 1-2. In addition, Examples 5 and 6 found on pages 21-23 of the specification illustrate how to make 3'-azido-3'-deoxy-5'-(3-dodecanamido-2-decyloxypropyl)-phosphothymidine and 3'-azido-3'-deoxy-5'-(dodecyoxy-2-decyloxypropyl)-phosphothymidine, which are exemplary compounds of Formula III. The structures of these Formula III compounds are as follows:

3'-azido-3'-deoxy-5'-(3-dodecanamido-2-decyloxypropyl)-phosphothymidine



3'-azido-3'-deoxy-5'-(dodecyoxy-2-decyloxypropyl)-phosphothymidine



In addition, in the Declaration of Kucera and the Kucera *et al.* article, which were previously submitted and copies of which are attached hereto, a working example of a compound of Formula III known as INK-14 is described. The INK-14 compound gave a high

selectivity index of >1250 against infectious HIV-1 replication in CEM-SS cells, as shown in Table 2 of Kucera *et al.*

In the specification, page 14, lines 20-21, Applicants state that experimentation demonstrated efficacy of the compounds of Formula III. Applicants describe that the compounds of Formula III can inhibit transport and/or incorporation of HIV-1 major glycoprotein gp120 in the cell membrane of an infected cell prior to viral assembly, where such inhibition blocks transmission of infectious HIV-1 into neighboring cells. Applicants further describe that compounds of Formula III can inhibit production of the HBV core and "e" antigens, each of which contribute to the assembly of new virus particles and the spread of HBV infection. Specification, page 14, line 30 - page 15, line 4.

The procedure for assessing anti-HIV-1 activity is described in the specification on page 23, line 27 - page 28, line 11 and the procedure for assessing HBV inhibition activity is described on page 25, lines 11-25. These procedures were well-known in the art at the time of the invention. Thus, at the time of the invention, one skilled in the art could have used these procedures, which are not undue, to demonstrate the efficacy of the compounds of Formula III.

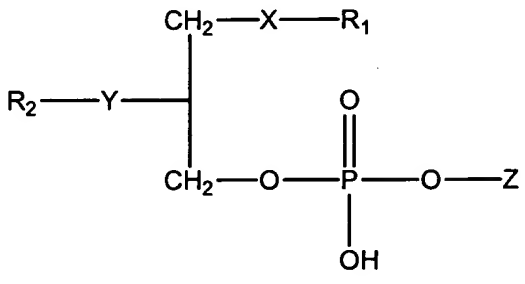
In view of the foregoing remarks and amendment, Claims 56-71, 95, 96, and 103-119, are fully enabled by the specification and the previously submitted Declaration of Kucera such that one of skill in the art would be able to make and use Applicants' claimed invention without undue experimentation. Therefore, Applicants respectfully request that this rejection be withdrawn.

III. Rejection under 35 U.S.C. §112, second paragraph

Claims 56-71, 95, 96 and 103-109 stand rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection.

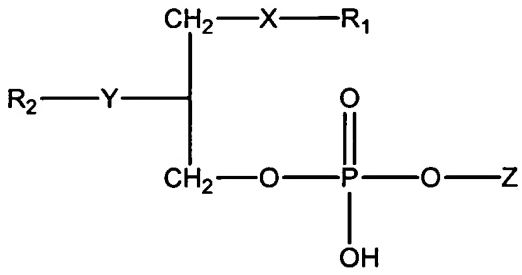
The Examiner stated that claims 56-71, 95, 96 and 103-109 are vague and indefinite in that it is not known what is meant by the compounds of Formula III, which contain an oxygen

atom with a negative charge without a balancing positive atom. To better clarify Applicants' invention, a hydrogen has been added to the oxygen atom as follows:



(III)

The Examiner also stated that claims 56-64, 67-71, 103, 104 and 107 are vague and indefinite in that it is not known what is meant by the definition of X which is missing part of the last moiety and is believed to be NCH_3. As set forth in claim 56, X is selected from the group of NHCO, CH_3NCO, S, SO, SO_2, O, NH and NCH_3. The last moiety, NH_3 would give a N-methylated tertiary amine as follows:

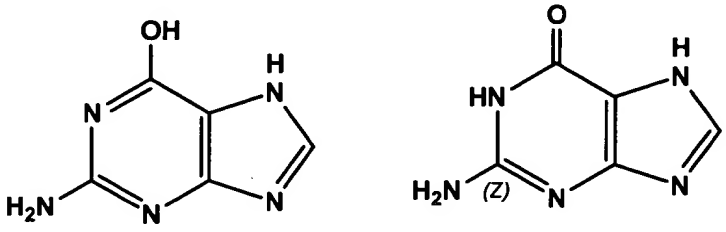


This moiety, NH_3 is not missing any parts.

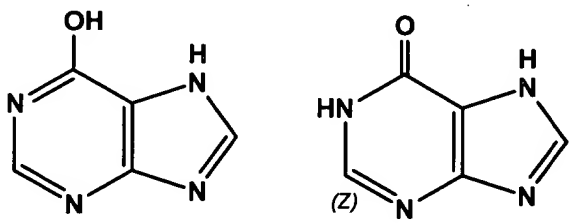
In addition, the Examiner stated that claims 56-67, 69-71, 95, 96 and 103-109 are vague and indefinite in that it is not known what is meant by the comma which appears after the structure of Formula (V) and before (V) on pages 3 and 4 of the amendment. To clarify Applicant's invention, the comma has been deleted.

The Examiner further stated that there is insufficient antecedent basis for the limitation "guanine, xanthine and hypoxanthine" in the definition of B in claim 68. The Examiner is correct that, as usually written, guanine and hypoxanthine require a carbonyl at position 6 and

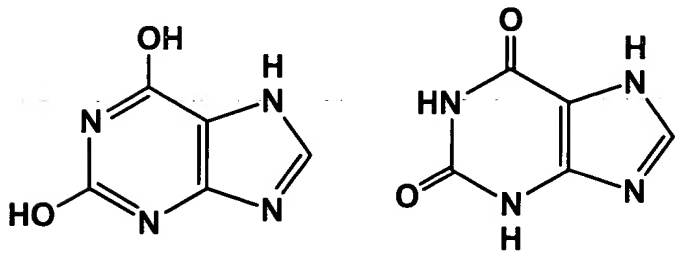
that xanthine requires a carbonyl at both positions 2 and 6 as is seen in the tautomeric forms below. However, as seen on the left, the tautomeric forms would be substituted with -OH at these positions, as is stated in the claim 68. When the pyrimidinyl moiety is substituted with -OH at position 6 or positions 2 and 6, the tautomeric form of -NH-C=O, rather than -N=C-OH, can be applied.



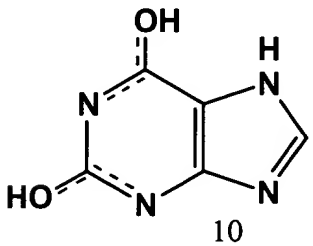
Tautomeric forms of Guanine



Tautomeric forms of Hypoxanthine



Tautomeric forms of Xanthine



Tautomeric forms with -N=C-OH & -NH-C=O at positions 2 & 6

In view of the foregoing remarks and amendment, claims 56-71, 95, 96 and 103-109, particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Thus, Applicants respectfully request that this rejection be withdrawn.

IV. Conclusion

Applicants respectfully request reconsideration of the subject application in view of the above amendments and remarks. The subject application is now in condition for allowance and early notice to that effect is respectfully solicited.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully submitted,

MORGAN, LEWIS & BOCKIUS LLP

By: _____
Kim R. Jessum
Reg. No. 43,694

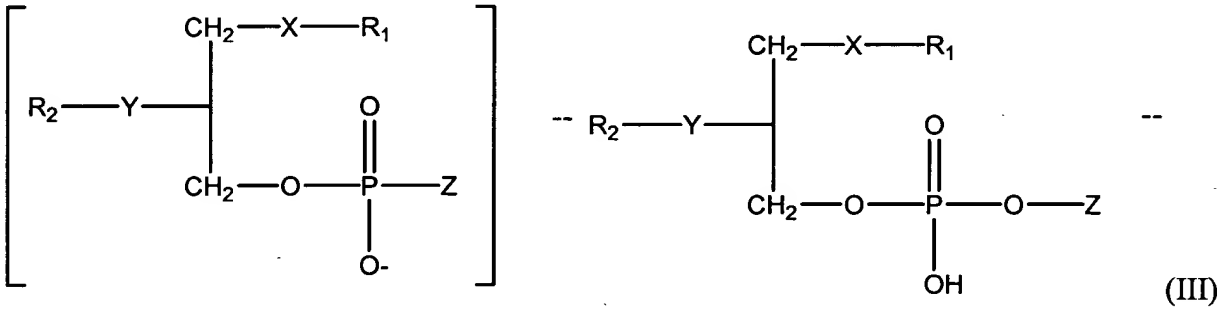
Dated: January 29, 2003
CUSTOMER NO. 028977
MORGAN, LEWIS & BOCKIUS LLP
1701 Market Street
Philadelphia, PA 19103-2921
(215) 963-5000

MARKED UP VERSION

In the Specification:

Please amend page 4, lines 5-15 as follows:

A third aspect of the present invention is a method of treating viral infections comprising administering to a subject in need of such treatment an effective infection-inhibiting amount of a compound of Formula III.



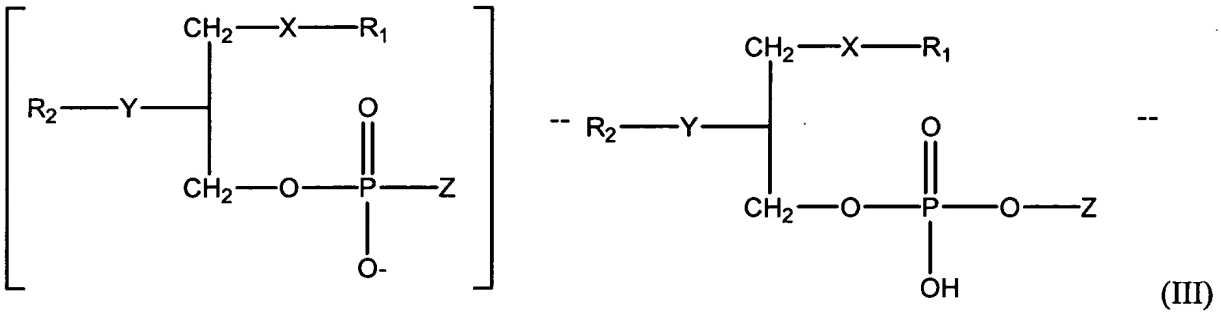
(III)

In the Claims:

Please amend claims 56 and 95 as follows:

56. (Twice Amended) A method of combating a viral infection in a subject in need of such treatment, wherein the viral infection comprises a virus selected from the group consisting of HIV-1, HBV, herpes virus, influenza, respiratory syncytial virus, mumps, measles, and parainfluenza virus, the method comprising administering to said subject an effective infection-combating amount of a compound of Formula III

Please replace Formula III on page 4, lines 8-15 as follows:



(III)

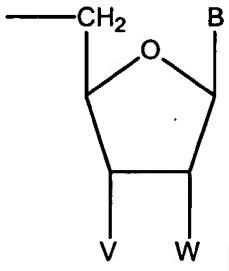
wherein: R_1 is a branched or unbranched, saturated or unsaturated C_6 to C_{18} alkyl group optionally substituted from 1 to 5 times with -OH, -COOH, oxo, amine, or substituted or unsubstituted aromatic;

X is selected from the group consisting of NHCO, CH_3NCO, CONH, $CONCH_3$, S, SO, SO_2, O, NH, and NCH_3;

R_2 is a branched or unbranched, saturated or unsaturated C_6 to C_{14} alkyl group optionally substituted from 1 to 5 times with -OH, -COOH, oxo, amine, or substituted or unsubstituted aromatic;

Y is selected from the group consisting of NHCO, CH_3NCO, CONH, $CONCH_3$, S, SO, SO_2, O, NH, and NCH_3; and

Z is a moiety of the Formula V,



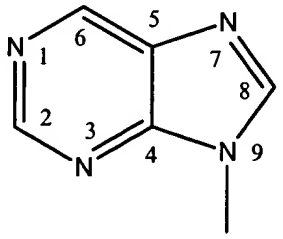
[,] (V)

wherein: V is H or N_3;

W is H or F; or

V and W together are a covalent bond; and

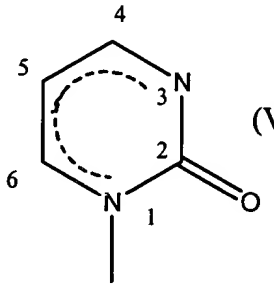
B is a purinyl moiety of Formula VI



(VI)

optionally substituted at position 2 with -OH, -SH, $-NH_2$ or halogen, at position 6 with Cl, $-NH_2$, -OH, or C_1-C_3 alkyl, and at position 8 with Br or I; or

B is a pyrimidinyl moiety of Formula VII



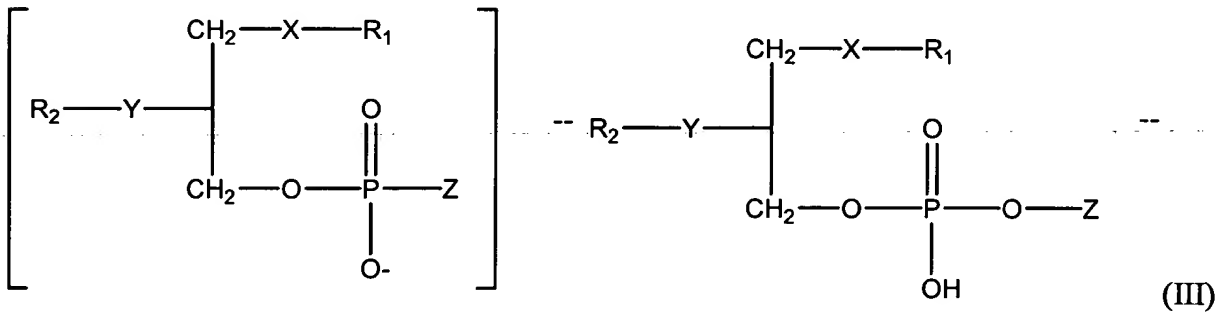
(VII)

substituted at position 4 with =O or NH_2 and optionally substituted at position 5 with halogen or C_1-C_3 saturated or unsaturated alkyl optionally substituted 1 to 3 times with halogen;

or a pharmaceutical salt thereof.

95. (Thrice Amended) A compound of Formula III

inhibiting amount of a compound of Formula III.



(III)

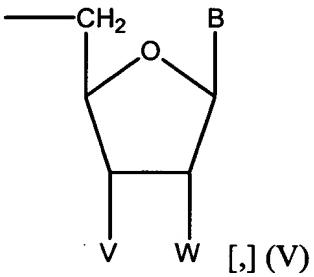
wherein: R_1 is a branched or unbranched, saturated or unsaturated C_6 to C_{18} alkyl group optionally substituted from 1 to 5 times with -OH, -COOH, oxo, amine, or substituted or unsubstituted aromatic;

X is selected from the group consisting of NHCO, CH_3NCO, CONH, $CONCH_3$, S, SO, SO_2, O, NH, and NCH_3;

R_2 is a branched or unbranched, saturated or unsaturated C_6 to C_{14} alkyl group optionally substituted from 1 to 5 times with -OH, -COOH, oxo, amine, or substituted or unsubstituted aromatic;

Y is selected from the group consisting of NHCO, CH_3NCO, CONH, $CONCH_3$, S, SO, SO_2, O, NH, and NCH_3; and

Z is a moiety of the Formula V,



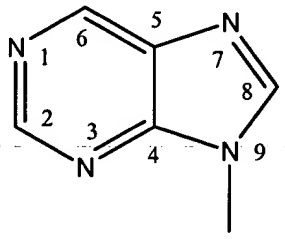
[,] (V)

wherein: V is H or N_3;

W is H or F; or

V and W together are a covalent bond; and

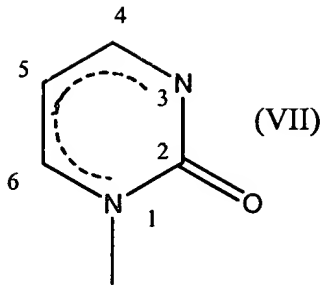
B is a purinyl moiety of Formula VI



(VI)

optionally substituted at position 2 with OH, -SH, $-NH_2$ or halogen, at position 6 with Cl, $-NH_2$, -OH, or C_1-C_3 alkyl, and at position 8 with Br or I; or

B is a pyrimidinyl moiety of Formula VII



(VII)

substituted at position 4 with =O or NH_2 and optionally substituted at position 5 with halogen or C_1-C_3 saturated or unsaturated alkyl optionally substituted 1 to 3 times with halogen.